



# UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
United States Patent and Trademark Office  
Address: COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/633,630	08/05/2003	Klaus Giese	39078-0005	6369
26633	7590	01/12/2006	EXAMINER	
HELLER EHRMAN WHITE & MCAULIFFE LLP 1717 RHODE ISLAND AVE, NW WASHINGTON, DC 20036-3001			CHONG, KIMBERLY	
			ART UNIT	PAPER NUMBER
			1635	

DATE MAILED: 01/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 10/633,630	<b>Applicant(s)</b> GIESE ET AL.	
	<b>Examiner</b> Kimberly Chong	<b>Art Unit</b> 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 28 October 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 11-23,25-27,29 and 31-33 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 11-23,25-27,29 and 31-33 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

## DETAILED ACTION

### *Status of Application/Amendment/Claims*

Applicant's response filed 10/28/2005 has been considered. Rejections and/or objections not reiterated from the previous office action mailed 06/28/2005 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

With entry of the amendment filed on 10/28/2005, claims 11-23, 25-27, 29 and 31-33 are pending and currently under examination. Applicant has canceled claims 1-10 and 24.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 11-23, 25-27, 29 and 31-33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 11 is drawn to a ribonucleic acid molecule comprising a double stranded structure having a first and second strand wherein the first strand comprises a first stretch of contiguous nucleotides and wherein the second strand comprises a second stretch of contiguous nucleotides

Art Unit: 1635

wherein said first stretch and/or said second stretch comprises a pattern of a plurality of groups of modified nucleotides having “a modification at the 2’-position.”

It is unclear which nucleotide in the group of modified nucleotides has “*a modification*” at the 2’-position. Do all the nucleotides in the group have a modification at the 2’-position or does just one nucleotide within the group have a modification at the 2’-position? Claims 2-23, 25-27, 29 and 31-33 are rejected as being dependent upon claim 11.

***Claim Rejections - 35 USC § 102***

For purpose of prior art, the word pattern is not specifically defined in the specification and therefore “pattern” is interpreted to mean “a configuration” of nucleotides (as defined in the Merriam Webster Dictionary 1997. 5<sup>th</sup> Ed.).

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 11-19, 25-27, 29 and 31-32 rejected under 35 U.S.C. 102(b) as being anticipated by Agrawal et al. (WO 94/01550).

Claim 11 is drawn to a ribonucleic acid molecule comprising a double stranded structure having a first and second strand wherein the first strand comprises a first stretch of contiguous nucleotides and wherein the second strand comprises a second stretch of contiguous nucleotides, wherein said first stretch and/or said second stretch comprises a pattern of a plurality of groups of modified nucleotides having a modification at the 2'-position, wherein each group of modified nucleotides with a stretch is flanked on one or both sides by a flanking group of unmodified or differently modified nucleotides. Claim 11 is further limited wherein each of said groups of modified or flanking nucleotides comprises one to ten nucleotides, wherein the pattern of modified nucleotides of said first stretch is the same as the pattern of modified nucleotides of said second stretch, the pattern of modification of said first stretch aligns or is shifted by one or more nucleotides with the pattern of modification of said second stretch, wherein the modification is selected from the group as listed in claim 16, wherein the double stranded structure is blunt ended at one or both ends, wherein at least one of the two strands has an overhang of at least one nucleotide at the 5'-end, wherein the complementarity between said first strand and the target nucleic acid is perfect, wherein the duplex formed between said first strand and the target nucleic acid comprises at least 15 nucleotides, the first and second strand are linked by a loop structure wherein the loop structure comprises a non-nucleotide acid polymer or is comprised of a nucleic acid, wherein ribonucleic acid is in a pharmaceutical composition and an organism comprising a cell and wherein the length of the double-stranded structure is from about 17 to 21 bases.

Agrawal et al. discloses a double stranded structure wherein the first strand comprises a first stretch of contiguous nucleotides that are perfectly complementary to target molecule (see

Art Unit: 1635

Figure 6) and wherein the double stranded structure is blunt ended on one or both ends or has at least one strand with an overhang (see Figure 5). Agrawal et al. further disclose the self-complementary region is linked by a loop structure wherein the loop structure comprises a nucleic acid or a non-nucleic acid linker (see page 15, lines 5-36). Agrawal et al. further disclose a ribonucleic acid comprising a self-complementary region wherein one or more ribonucleotides are modified at the 2'-position with a methoxy (see page 16, lines 5-30). The ribonucleic acid disclosed by Agrawal et al. comprises a double stranded structure wherein only one ribonucleotide is modified at the 2'-position; therefore the modified ribonucleotide is flanked by unmodified ribonucleotides forming a pattern wherein the self-complementary regions align. It must be noted that the specification does not define "aligns". Align is defined as "to bring into a line" (see page 36, Merriam Webster Dictionary 1997, 5<sup>th</sup> Ed.) and therefore in the context of double stranded nucleic acid sequences, alignment a first nucleotide strand with a second nucleotide strand is based on the complementarity of the sequences and not a specific pattern of nucleotides. Agrawal et al. further disclose a ribonucleic acid and a pharmaceutical acceptable carrier and further discloses a cell comprising a ribonucleic acid (see page 18, lines 1-14 and Example 3).

Thus, Agrawal et al. anticipates claims 11-19, 25-27, 29 and 31-32 of the instant application.

Claims 11-16 and 21-23 are rejected under 35 U.S.C. 102(b) as being anticipated by Crooke et al. (U.S. Patent No. 6,107,094).

Claim 11 is drawn to a ribonucleic acid molecule comprising a double stranded structure having a first and second strand wherein the first strand comprises a first stretch of contiguous nucleotides and wherein the second strand comprises a second stretch of contiguous nucleotides, wherein said first stretch and/or said second stretch comprises a pattern of a plurality of groups of modified nucleotides having a modification at the 2'-position, wherein each group of modified nucleotides with a stretch is flanked on one or both sides by a flanking group of unmodified or differently modified nucleotides. Claim 11 is further limited wherein each of said groups of modified or flanking nucleotides comprises one to ten nucleotides, wherein the pattern of modified nucleotides of said first stretch is the same as the pattern of modified nucleotides of said second stretch, the pattern of modification of said first stretch aligns or is shifted by one or more nucleotides with the pattern of modification of said second stretch, wherein the modification is selected from the group as listed in claim 16 and further wherein the length of the double-stranded structure is from about 17 to 21 bases.

Crooke et al. discloses a ribonucleic acid comprising a double stranded structure wherein the first and second strands comprise a first stretch of contiguous nucleotides that are at least partially or perfectly complementary to target molecule and wherein the double stranded structure is between 17-20 nucleotides (see Table 1). Crooke et al. further discloses a double stranded structure comprising "a pattern of a plurality of groups of modified nucleotides" modified at the 2'-position with a methoxy and flanked by unmodified nucleotides that consist of one to ten nucleotides and wherein the two strands align (see Table 1). It must be noted that the specification does not define "aligns". Align is defined as "to bring into a line" (see page 36, Merriam Webster Dictionary 1997, 5<sup>th</sup> Ed.) and therefore in the context of double stranded

Art Unit: 1635

nucleic acid sequences, alignment a first nucleotide strand with a second nucleotide strand is based on the complementarity of the sequences and not a specific pattern of nucleotides.

Thus, Crooke et al. anticipates claims 11-16 and 21-23 of the instant application.

Claims 11-20, 29 and 31-33 are rejected under 35 U.S.C. 102(e) as being anticipated by Tuschl et al. (WO 02/44321).

Claim 11 is drawn to a ribonucleic acid molecule comprising a double stranded structure having a first and second strand wherein the first strand comprises a first stretch of contiguous nucleotides and wherein the second strand comprises a second stretch of contiguous nucleotides, wherein said first stretch and/or said second stretch comprises a pattern of a plurality of groups of modified nucleotides having a modification at the 2'-position, wherein each group of modified nucleotides with a stretch is flanked on one or both sides by a flanking group of unmodified or differently modified nucleotides. Claim 11 is further limited wherein each of said groups of modified or flanking nucleotides comprises one to ten nucleotides, wherein the pattern of modified nucleotides of said first stretch is the same as the pattern of modified nucleotides of said second stretch, the pattern of modification of said first stretch aligns or is shifted by one or more nucleotides with the pattern of modification of said second stretch, wherein the modification is selected from the group as listed in claim 16, wherein the double stranded structure is blunt ended at one or both ends, wherein at least one of the two strands has an overhang of at least one nucleotide at the 5'-end, wherein the complementarity between said first strand and the target nucleic acid is perfect, wherein the duplex formed between said first strand and the target nucleic acid comprises at least 15 nucleotides, the first and second strand are



Art Unit: 1635

linked by a loop structure wherein the loop structure comprises a non-nucleotide acid polymer or is comprised of a nucleic acid, wherein ribonucleic acid is in a pharmaceutical composition and an organism comprising a cell and wherein the length of the double-stranded structure is from about 17 to 21 bases.

Tuschl et al. discloses a double stranded structure wherein the first and second strands comprise a first stretch of contiguous nucleotides that are at least partially or perfectly complementary to target molecule (see page 6, lines 7-16) and wherein the double stranded structure is between 17-25 nucleotides, is blunt ended on one or both ends or has at least one strand with an overhang (see page 4 lines 1-20). Tuschl et al. further discloses a double stranded structure comprising "a pattern of a plurality of groups of modified nucleotides", namely two or four nucleotides modified at the 2'-position with a methoxy, wherein the group is flanked by unmodified nucleotides that consist of one to ten nucleotides (see Figure 14) and further the pattern of two or four nucleotides modified at the 2'-position on the first strand is the same as the pattern on the second strand wherein the two strands align. It must be noted that the specification does not define "aligns". Align is defined as "to bring into a line" (see page 36, Merriam Webster Dictionary 1997, 5<sup>th</sup> Ed.) and therefore in the context of double stranded nucleic acid sequences, alignment of a first nucleotide strand with a second nucleotide strand is based on the complementarity of the sequences and not a specific pattern of nucleotides. Tuschl et al. further teach a ribonucleic acid wherein the duplex formed between the first strand and the target is at least 15 nucleotides and wherein there are one or two mismatches between the first strand and the target (see Figure 18). Tuschl et al. further disclose a ribonucleic acid in a pharmaceutical

Art Unit: 1635

composition (see paragraph 0031) and a cell in an organism comprising the ribonucleic acid (see paragraph 0028).

Thus, Tuschl et al. anticipates claims 11-20, 29 and 31-33 of the instant application.

Claims 11-19, 21-23, 25-27, 29 and 31-33 rejected under 35 U.S.C. 102(e) as being anticipated by McSwiggen et al. (US 2003/0190635).

Claim 11 is drawn to a ribonucleic acid molecule comprising a double stranded structure having a first and second strand wherein the first strand comprises a first stretch of contiguous nucleotides and wherein the second strand comprises a second stretch of contiguous nucleotides, wherein said first stretch and/or said second stretch comprises a pattern of a plurality of groups of modified nucleotides having a modification at the 2'-position, wherein each group of modified nucleotides with a stretch is flanked on one or both sides by a flanking group of unmodified or differently modified nucleotides. Claim 11 is further limited wherein each of said groups of modified or flanking nucleotides comprises one to ten nucleotides, wherein the pattern of modified nucleotides of said first stretch is the same as the pattern of modified nucleotides of said second stretch, the pattern of modification of said first stretch aligns or is shifted by one or more nucleotides with the pattern of modification of said second stretch, wherein the modification is selected from the group as listed in claim 16, wherein the double stranded structure is blunt ended at one or both ends, wherein at least one of the two strands has an overhang of at least one nucleotide at the 5'-end, wherein the complementarity between said first strand and the target nucleic acid is perfect, wherein the duplex formed between said first strand and the target nucleic acid comprises at least 15 nucleotides, the first and second strand are

Art Unit: 1635

linked by a loop structure wherein the loop structure comprises a non-nucleotide acid polymer or is comprised of a nucleic acid, wherein ribonucleic acid is in a pharmaceutical composition and an organism comprising a cell and wherein the length of the double-stranded structure is from about 17 to 21 bases.

McSwiggen et al. discloses a ribonucleic acid comprising a double stranded structure wherein the first and second strands comprise a first stretch of contiguous nucleotides that are at least partially or perfectly complementary to target molecule (see paragraph 0017 and 0121) and wherein the double stranded structure is between 19-25 nucleotides (see paragraph 0035).

McSwiggen et al. further discloses the double stranded structure comprises “a pattern of a plurality of groups” of 2'-modified nucleotides, flanked by modified or unmodified nucleotides that consist of one to ten nucleotides and the modification at the 2' position can comprise a methoxy or fluoro wherein the two strands are aligned (see Figure 5). It must be noted that the specification does not define “aligns”. Align is defined as “to bring into a line” (see page 36, Merriam Webster Dictionary 1997, 5<sup>th</sup> Ed.) and therefore in the context of double stranded nucleic acid sequences, alignment of a first nucleotide strand with a second nucleotide strand is based on the complementarity of the sequences and not a specific pattern of nucleotides.

McSwiggen et al. further disclose a double stranded structure wherein the pattern of modifications are the same on both strands, the modified nucleotide on the first strand is complementary with an unmodified nucleotide on the second strand, the terminal 5' nucleotide of the first strand is modified and the terminal 3' nucleotide of the second strands is a flanking nucleotide and further wherein the modified nucleotide is on the 5' end relative to the flanking unmodified nucleotide (see Figure 5). McSwiggen et al. further disclose the ribonucleic acid

Art Unit: 1635

first and second strand are linked by a loop structure wherein the loop structure can be a nucleotide of a non-nucleotide linker (see paragraph 0017 and Figure 6). McSwiggen et al. further disclose a ribonucleic acid in a pharmaceutical composition (see paragraph 00198) and a cell in an organism comprising the ribonucleic acid (see paragraph 0027).

Thus, McSwiggen et al. anticipates claims 11-19, 21-23, 25-27, 29 and 31-33 of the instant application.

### *Response to Applicant's Arguments*

The rejection of record of claims 1-27, 29 and 31-32 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in response to Applicant's amendments filed 10/28/2005.

The rejection of record of claims 1-7, 9-10, 19, 24, 29 and 31-32 rejected under 35 U.S.C. 102(b) as being anticipated by Kool (US Patent No. 5,514,546) is withdrawn in response to Applicant's amendments filed 10/28/2005.

The rejection of record of claims 1-7, 9-12, 16-19, 29 and 31-32 rejected under 35 U.S.C. 102(e) as being anticipated by Tuschl et al. (US 2004/0229266) is withdrawn in response to Applicant's amendments filed 10/28/2005.

The rejection of record of claims 1-10, 19-20, 24, 29 and 31-32 under rejected under 35 U.S.C. 103(a) as being unpatentable over Kool (US Patent No. 5,514,546) in view of Beigelman

Art Unit: 1635

et al. (US Patent No. 6,617,438) and further in view of Holen et al. (Nucleic Acids Research, 2002: Vol. 30, No. 8) is withdrawn in response to Applicant's amendments filed 10/28/2005.

The rejection of record of claims 1-3, 7-8, 10-14, 16-17, 19, 21-25-27, 29 and 31-32 rejected under 35 U.S.C. 103(a) as being unpatentable over McSwiggen et al. (US 2003/0190635) in view of Crooke et al. (US Patent No. 5,898,031) and in further view of Kool (US Patent No. 5,514,546) is withdrawn in response to Applicant's amendments filed 10/28/2005.

### **Conclusion**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly Chong whose telephone number is 571-272-3111. The examiner can normally be reached Monday thru Friday between 7-4 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached at 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system

Art Unit: 1635

provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For more information about the PAIR system, see <http://pair-direct.uspto.gov>.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Kimberly Chong  
Examiner  
Art Unit 1635



SEAN MCGARRY  
PRIMARY EXAMINER  
1635